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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,989	11/03/2005	Hesson Chung	HANO-004	1940

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BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,989	CHUNG ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11,12,17-19,21-31,35,36,41-44 and 46-58* is/are pending in the application.

4a) Of the above claim(s) *1-7,11,12,17-19,21-25 and 48-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-31,35,36,41-44,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *18 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 Nov 2005 and 26 Mae 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO REMARKS

The Examiner thanks the Applicants for their timely reply filed on 18 June 2008, in the matter of 10/521,989.

Applicants' election **with traverse** of Group III (claims 26-31, 35, 36, 41-44, 46 and 47) is acknowledged. Applicants request reconsideration of the lack of unity requirement on the grounds that "it would not be unduly burdensome to perform a search on all of the claims together in the present application".

Applicants' request for reconsideration of the lack of unity requirement has been fully considered by the Examiner and **is persuasive in part.** However, after further consideration of the prior art, a lack of unity remains wherein the inventions listed in Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features. This is evidenced by the co-pending application (US Pre-Grant Publication No. 2006/0104999) to Chung et al. which expressly teach a paclitaxel-specific embodiment of the instantly claimed generic composition (see claims 1, 5, 6, 10-12, 27, 33, 37, 38, 42, 43, 48-51 and 72-74).

Applicants' elections of Group III stand and are made **FINAL**. The claims of Groups I, II and IV-VI are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Applicants timely traversed the restriction requirement between the compositions and methods.

The remaining claims 26-31, 35, 36, 41-44, 46 and 47 are presented and represent all claims under consideration.

INFORMATION DISCLOSURE STATEMENT

Two Information Disclosure Statements (IDS), filed 3 November 2005 and 26 March 2007, are acknowledged and have been reviewed.

SPECIFICATION

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-31, 35, 36, 41-44, 46 and 47 are is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 26, 27, 30 and 42, percentage ranges for each of the components are recited using the symbol "~". Recitation of the ranges using said symbol renders the claims indefinite because the symbol has a well-known connotative definition of meaning "approximately" or "about". Thus is it is unclear exactly what compositional ranges Applicant is reciting.

The remaining claims are rejected since they depend from rejected claims.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 26-30, 35, 36, 41-43, 46 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Carrier et al. (WO 99/49848).

The instant claims are directed to a mucoadhesive formulation comprising, by weight, 4-90% of at least one monoglyceride compound, 0.01-90% of at least one oil and 0.01-20% of at least one insoluble drug (claim 26 and 46). The administration route limitation in claim 46 is considered by the Examiner to be a recitation of intended use, since said limitation does not serve to further limit the actual composition. Additional components such as 0.01-90% of at least one emulsifier and 0.01-5% of an additive are recited (claims 27 and 42, respectively). Claims 35 and 36 further limit the emulsifier compound. Claim 28 further limits the monoglyceride component. Additional limitations to the oil component are recited in claims 29-31. General categories of drug types are recited in claim 41. Claims 43 and 44 further limit the additive component. Claim 47 recites that the formulation be either liquid or semi-solid.

Carrier et al. teach an orally administrable pharmaceutical composition comprising an **anticancer drug** as an active ingredient dissolved in a carrier system comprising at least one hydrophobic component and at least one surfactant (claims 1 and 17). Example 5 teaches a

specific embodiment comprising **paclitaxel** (1.4% by weight), the **emulsifier Tween 80** (43% by weight), the **caprylic/capric triglyceride** Miglyol 812 as the oil (28.7% by weight), and **soybean oil as a monoglyceride semi-synthesized from triglycerides of vegetable oil** (3.6% by weight). Example 5 also teaches the presence of additives such as linoleic acid (3.4% by weight) as well as ethanol (6.1% by weight). All compositions of the Examples to Carrier et al. are taught as resulting in a liquid or semi-solid pre-concentrate formulation (page 7, lines 22-23).

Claims 26-31, 35, 36, 41-44, 46 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Chung et al. (US Pre-Grant Application No. 2006/0104999).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The invention to Chung et al. teaches a composition comprising, by weight, 0.01-20% of the insoluble anti-cancer drug paclitaxel, 4-90% of at least one monoolein, 0.01-90% of an oil such as a triglyceride, an iodized, a vegetable or an animal oil, and 0.01-90% of an emulsifier (claim 33). Claim 74 teaches the composition of claim 33 as being in liquid or semi-solid state. Claim 37 teaches that the triglyceride is chosen from saturated and unsaturated triglycerides having 2-20 carbon atoms in each chain. Claim 38 expressly teaches the recited limitations to the triglycerides, iodized, vegetable and animal oils. Claims 42 and 43 teach the claimed categories of

emulsifiers and the more specific embodiments of each, respectively. Claims 48 and 49 teach the inclusion of 0.01-5% by weight of other additives such as alcohols and polyols. Claim 50 specifically teaches the claimed alcohol and polyol additives. Claim 46 teaches the instantly claimed intended uses (i.e. routes of administration) of the composition. Therefore, each and every one of the limitations has been met by the reference.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26-31, 35, 36, 41-44, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woo et al. (WO 02/13815).

The instant claims are directed to a mucoadhesive formulation, as discussed above.

Woo et al. teach an oral composition comprising an insoluble drug, emulsifier (e.g. surfactant) and an oil (claims 1, 2 and 6). Claims 2 and 3 teach paclitaxel as the insoluble drug. Claim 7 teaches the following weight ratio ranges: 1-100 for the additive (e.g. co-surfactant), 5-100 for the emulsifier (e.g. surfactant), and 1-100 for the oil, all of which are based on 1 part by weight of the drug. Claim 8 teaches ethanol and/or polyethylene glycol as additives. Claim 9 teaches the emulsifier as comprising such compounds as polyoxyethylene-polyoxypropylene copolymer and monoglycerides. Claim 10 teaches the oil as comprising such compounds as squalene and squalane. Monoglycerides are taught in claims 9 and 10 as well as on pages 5 and 6, as other forms of emulsifiers and/or oils. The monoglyceride glyceryl monoleate is expressly taught in the formulation of Example 8. For example, a preferred monoglyceride prepared from oleic acid is taught (pg. 6, lines 18-19). Triglycerides are similarly taught as oil components in the form of fatty acid triglycerides such as fractionated coconut oil (pg. 6, lines 16-17). Formulation of the composition into a dissolved or liquid state such as a solution, emulsion or micro-emulsion, is the preferred route particularly since the liquid composition is taught as being used to fill hard and soft gelatin capsules (page 7, lines 14-21).

Neither the claimed percent ranges for components nor the 2-20 carbon atom triglyceride compounds, as instantly claimed are expressly taught by Woo et al.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising an insoluble drug, a monoglyceride, an oil, an emulsifier and an additional additive, as suggested by Woo, modify the amounts and ratios of the ingredients, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Woo expressly teaches composition embodiments which comprise an insoluble drug such as paclitaxel, admixed with emulsifiers, oils and additives. Triglycerides, while not being taught as expressly as the other claimed ingredients of the composition, are taught as components used as or in combination with the emulsifiers (e.g. surfactants) and/or the oils (pg. 5 and 6). While the reference does not expressly teach ranges, as claimed by Applicants, the values and formats of each parameter with respect to the claimed composition are adjustable. It thus follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. In the instant case, it would have been within the purview of the skilled artisan to adjust the amount and type of monoglyceride and/or triglyceride compounds used in the composition. Thus, it would have been customary for an artisan of ordinary skill, to adjust percent ranges of the components in the composition, in order to achieve the desired mucoadhesive formulation. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the

invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Claims 26-31, 35, 36, 41-44, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carrier et al. (WO 99/49848).

The instant claims are directed to a mucoadhesive formulation, as discussed above.

The teachings to Carrier et al. are discussed above, as well.

Carrier does not expressly teach in the claims or Examples the use of specific types of triglycerides (i.e. vegetable oils) or the specific percent amount of alcohol or polyol additive within the composition.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising an insoluble drug, a monoglyceride, an oil, an emulsifier and an additional additive, as suggested by Carrier, modify the amounts and ratios of the ingredients, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Carrier teaches that the compound used as an oil in Example 5, namely Miglyol 812, is functionally equivalent to many other hydrophobic compounds such as vegetable oils (e.g. olive, corn and soybean). Similarly, Example 5 teaches the prepared composition as containing 6.1% of the additive ethanol; just outside of the instantly claimed range for the additive. One with ordinary skill in the art would substitute and/or vary the levels of these materials, within the ranges taught

by Carrier, during the process of routine experimentation in order to optimize the fluidity and stability of the composition.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-31, 35, 36, 41-44, 46 and 47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33, 37, 38, 42, 43, 48-51, 65 and 74 of copending Application No. 10/521,669 (US Pre-Grant Publication No. 2006/0104999). Although the conflicting claims are not identical, they are not patentably distinct

from each other because the copending claims of the '669 application are obvious variants, if not anticipatory, of the currently presented claims. The subject matter recited by both the instant claims 26-29 and 41 is combined within and read upon by claim 33 of the '669 application. Instant claims 30 and 31 are read on and anticipated by copending claims 37 and 38 regarding the specific triglyceride and oil components. Instant claims 35 and 36 are read on and anticipated by copending claims 42 and 43 regarding the emulsifier limitations. Instant claims 42-44 are read on and anticipated by copending claims 48-50 regarding the additive limitations. Instant claims 46 and 47 are read on and anticipated by copending claims 65 and 74, regarding routes of administration and liquid/semi-solid form limitations, respectively. The key difference in subject matter between the copending claims and the instant claims is that the claims to the '669 application specifically recite anti-cancer drugs such as paclitaxel and doxorubicin (claim 51). Despite the aforementioned difference, one of ordinary skill in the art would have immediately recognized the anticipatory and obvious overlap in subject matter and would have been motivated with a high expectation of success, to prepare the instantly claimed composition.

Claims 26-31, 35, 36, 41-44, 46 and 47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 10, 11 and 16-19 of copending Application No. 10/521,695 (US Pre-Grant Publication No. 2006/0127420). Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims of the '695 application are obvious variants, if not anticipatory, of the currently presented claims. The subject matter recited by both the instant claims 26, 27, 41, 46 and 47 is combined within and read upon by claim 1 of the '695 application. Instant claims 30

and 31 are read on and anticipated by copending claims 5 and 6 regarding the specific triglyceride and oil components. Instant claims 35 and 36 are read on and anticipated by copending claims 10 and 11 regarding the emulsifier limitations. Instant claims 42-44 are read on and anticipated by copending claims 16-18 regarding the additive limitations. Instant claims 46 and 47 are read on and rendered obvious by copending claims 1, regarding routes of administration and liquid/semi-solid form limitations, respectively, particularly in view of the fact that the composition is claimed as being for treatment of a bladder tumor, which necessitates the subcutaneous injection of a liquid form of the composition to reach said tumor. The key difference in subject matter between the copending claims and the instant claims, again, is that the claims to the '695 application specifically recite anti-cancer drugs such as paclitaxel (claim 1) and others such as doxorubicin (claim 19). Despite the aforementioned difference, one of ordinary skill in the art would have immediately recognized the anticipatory and obvious overlap in subject matter and would have been motivated with a high expectation of success, to prepare the instantly claimed composition.

These are provisional obviousness-type double patenting rejections because the claims in each of the conflicting cases have in fact not yet been patented.

All claims have been rejected; no claims are allowed.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615